

Citation:

Joshipura KJ, Hung HC, Li TY, Hu FB, Rimm EB, Stampfer MJ, Colditz G, Willett WC. Intakes of fruits, vegetables and carbohydrate and the risk of CVD. *Public Health Nutr.* 2009 Jan; 12(1): 115-121.

PubMed ID: [18410704](#)

Study Design:

Prospective Cohort Study

Class:

B - [Click here](#) for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To prospectively evaluate the association between intakes of total and specific fruits and vegetables and incidence of cardiovascular disease (CVD) among people with low carbohydrate intake.

Inclusion Criteria:

- Nurses Health Study (NHS) participants: Nurses aged 30 to 55 years recruited in 1976
- Health Professionals' Follow-Up Study (HPFS) participants: Health professionals aged 40 to 75 years recruited in 1986.

Exclusion Criteria:

Participants with incomplete or implausible dietary assessments or with cancer, diabetes or CVD that was reported before the baseline dietary assessment.

Description of Study Protocol:**Recruitment**

NHS and HPFS participants.

Design

Prospective cohort study.

Dietary Intake/Dietary Assessment Methodology

Participants reported their average frequency of intake of the specified standard serving or portion

size for each food over the past year.

Statistical Analysis

- Three groups were defined based on the percentage of energy derived from carbohydrate (low, less than 40%; moderate, less than 40% to 55%; and high, less than 55%)
- Cox proportional hazards regression analysis was used to assess whether a high intake of total or specific fruits and vegetables was associated with reduced risk of ischemic CVD among the three carbohydrate intake groups
- Analyses was performed separately for each cohort, and the results were also pooled to obtain overall estimates
- For the categorical analyses, the lowest quintile of intake formed the reference category
- The relative risk for the continuous measures was calculated and adjusted for standard CVD risk factors
- For each two-year follow-up period in which events were reported, the intake for each composite item was computed as a cumulative average of intake from all available food-frequency questionnaires (FFQ) up to the start of the follow-up period.

Data Collection Summary:

Timing of Measurements

- The baseline dietary assessment was in 1984 for the NHS and 1986 for the HPFS
- Additional mailed questionnaires were completed 1986, 1990, 1994, and 1998 for the NHS and 1990, 1994, and 1998 for the HPFS
- Study end date was June 1, 2000.

Dependent Variables

Ischemic heart disease, which included fatal CVD or non-fatal myocardial infarction and fatal or nonfatal ischemic stroke (excluding hemorrhagic strokes or strokes of unknown type), and included both confirmed and probable cases through medical record review

Independent Variables

- Fruit and vegetable intake (average frequency of intake of the specified standard serving/portion size for each food over the past year)
- Percentage of energy intake from carbohydrate (three groups)

Control Variables

- Total energy intake
- Whole grains
- Age
- Smoking
- Alcohol
- Body mass index (BMI)
- Multivitamin and vitamin E supplement use
- Aspirin use
- Physical activity
- Family history of myocardial infarction
- History of hypertension

- Hypercholesterolemia
- Incident diabetes
- Menopausal status
- Hormone replacement therapy (HRT).

Description of Actual Data Sample:

- *Initial N*: 121,700 women and 51,529 men in the original cohorts
- *Attrition (final N)*: 70,870 women and 38,918 women
- *Age*: Women and men were aged 30 to 55 years and 40 to 75 years, respectively, at study recruitment
- *Other relevant demographics*: High socioeconomic populations
- *Location*: US.

Summary of Results:

Key Findings

- Total fruits and vegetables showed a small non-significant inverse association among men and women with low energy-adjusted carbohydrate intake, with a pooled relative risk (RR) for an increment of five servings per day of 0.81 (95% CI: 0.65 to 1.01)
- When comparing extreme quantiles of fruits and vegetables, a small insignificant association was also seen in the low carbohydrate group (RR=0.73; 95% CI: 0.51 to 1.04)
- Total fruit showed the strongest inverse association among the moderate carbohydrate group when comparing extreme quantiles (RR=0.81; 95% CI: 0.70, 0.94). No significant linear association was found in any of the carbohydrate intake groups
- The linear trend was significant for total vegetables in the low carbohydrate group, with a pooled risk ratio for three servings a day of 0.82 (95% CI=0.68, 0.99, P=0.04)
- For the group with both high fruit and vegetable (more than five servings per day) and high carbohydrate intake (more than 50% of energy from carbohydrate), the low fruit and vegetable intake and high carbohydrate group showed an increase in cardiovascular disease for men (RR=1.21; 95% CI=1.02, 1.42), but not for women
- After adjustment for fruits and vegetables, there was no relationship between high carbohydrate intake and ischemic cardiovascular disease.

Author Conclusion:

Total fruit and vegetable intake had a small, insignificant association with ischemic cardiovascular disease among persons with low carbohydrate intake and no association among moderate and high carbohydrate intake groups. This inverse association was primarily due to vegetable intake.

Reviewer Comments:

- *Strengths*:
 - *Multivariable analysis with adjustment for many covariates*
 - *Medical record outcome assessment*
 - *Information on exposures updated throughout follow-up*
- *Limitation: Fruit and vegetable intake was self-reported and estimated over the past year.*

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

- | | | |
|----|---|-----|
| 1. | Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies) | Yes |
| 2. | Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about? | Yes |
| 3. | Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice? | Yes |
| 4. | Is the intervention or procedure feasible? (NA for some epidemiological studies) | Yes |

Validity Questions

- | | | |
|------|---|-----|
| 1. | Was the research question clearly stated? | Yes |
| 1.1. | Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified? | Yes |
| 1.2. | Was (were) the outcome(s) [dependent variable(s)] clearly indicated? | Yes |
| 1.3. | Were the target population and setting specified? | Yes |
| 2. | Was the selection of study subjects/patients free from bias? | Yes |
| 2.1. | Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study? | Yes |
| 2.2. | Were criteria applied equally to all study groups? | Yes |
| 2.3. | Were health, demographics, and other characteristics of subjects described? | Yes |
| 2.4. | Were the subjects/patients a representative sample of the relevant population? | Yes |
| 3. | Were study groups comparable? | Yes |
| 3.1. | Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT) | N/A |
| 3.2. | Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline? | N/A |
| 3.3. | Were concurrent controls used? (Concurrent preferred over historical controls.) | Yes |

3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	Yes
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	Was method of handling withdrawals described?	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	N/A
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	N/A
4.4.	Were reasons for withdrawals similar across groups?	N/A
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	Was blinding used to prevent introduction of bias?	N/A
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	N/A
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were intervening factors described?	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes

6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	N/A
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	Were outcomes clearly defined and the measurements valid and reliable?	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	Was the statistical analysis appropriate for the study design and type of outcome indicators?	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	Yes

8.7.	If negative findings, was a power calculation reported to address type 2 error?	No
9.	Are conclusions supported by results with biases and limitations taken into consideration?	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	Is bias due to study's funding or sponsorship unlikely?	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes